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A STUDY OF HUMAN ACCLIMATIZATION TO HYPOBARIC HYPOXIA

FINAL REPORT

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MARCH 1, 1987

~~NOVEMBER 20, 1986~~

Supported by:

U.S ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND  
Fort Detrick, Frederick, Maryland 21701-5012

CONTRACT No. DAMD17-85-C-5206

The Arctic Institute of North America  
Washington, DC 20007 and Calgary, Alberta

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## SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188									
1a. REPORT SECURITY CLASSIFICATION Unclassified		1b. RESTRICTIVE MARKINGS											
2a. SECURITY CLASSIFICATION AUTHORITY		3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution unlimited											
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE													
4. PERFORMING ORGANIZATION REPORT NUMBER(S)		5. MONITORING ORGANIZATION REPORT NUMBER(S)											
6a. NAME OF PERFORMING ORGANIZATION The Arctic Institute of North America		6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION										
6c. ADDRESS (City, State, and ZIP Code) Washington, DC 20007		7b. ADDRESS (City, State, and ZIP Code)											
8a. NAME OF FUNDING/SPONSORING ORGANIZATION U.S. Army Medical Research & Development Command		8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER DAMD17-85-C-5206										
8c. ADDRESS (City, State, and ZIP Code) Fort Detrick Frederick, MD 21701-5012		10. SOURCE OF FUNDING NUMBERS <table border="1"><tr><td>PROGRAM ELEMENT NO.</td><td>PROJECT NO.</td><td>TASK NO.</td><td>WORK UNIT ACCESSION NO.</td></tr><tr><td>62777A</td><td>3E1-62777A879</td><td>BC</td><td>097</td></tr></table>			PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.	62777A	3E1-62777A879	BC	097	
PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.										
62777A	3E1-62777A879	BC	097										
11. TITLE (Include Security Classification) (U) A Study of Human Acclimatization to Hypobaric Hypoxia													
12. PERSONAL AUTHOR(S) Charles S. Houston, John R. Sutton, and Allen Cymerman													
13a. TYPE OF REPORT Final	13b. TIME COVERED FROM 8/5/85 TO 2/15/87		14. DATE OF REPORT (Year, Month, Day) 1987 March 1	15. PAGE COUNT									
16. SUPPLEMENTARY NOTATION													
17. COSATI CODES <table border="1"><tr><th>FIELD</th><th>GROUP</th><th>SUB-GROUP</th></tr><tr><td>06</td><td>04</td><td></td></tr><tr><td>06</td><td>05</td><td></td></tr></table>		FIELD	GROUP	SUB-GROUP	06	04		06	05		18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number) RA 3,		
FIELD	GROUP	SUB-GROUP											
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19. ABSTRACT (Continue on reverse if necessary and identify by block number)  In the fall of 1985 eight male subjects lived for 45 days in a decompression chamber while the atmospheric pressure in the chamber was gradually reduced to simulate an ascent of Mt. Everest 8848 m, 29,028 ft. The purpose of the study was to examine all parts of the oxygen transport system during acclimatization to hypobaric hypoxia in an environment where the confounding stresses experienced on high mountains would be absent. Many chamber studies have defined the responses to acute exposure to high altitude, which are of great importance and interest to military and civilian aviators, as well as to millions of visitors to mountain resorts, but there have been few studies of acclimatization under the controlled conditions possible in the chamber. (AU)													
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input type="checkbox"/> UNCLASSIFIED/UNLIMITED <input checked="" type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS		21. ABSTRACT SECURITY CLASSIFICATION Unclassified											
22a. NAME OF RESPONSIBLE INDIVIDUAL Mary Frances Bostian		22b. TELEPHONE (Include Area Code) 301-663-7325	22c. OFFICE SYMBOL SGRD-RMI-S										

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FOREWORD

For the protection of human subjects the investigator(s)  
have adhered to policies of applicable Federal Law 45CFR46.

## HISTORICAL BACKGROUND

Adaptation of natives born to generations resident at high altitude has been recognized for many years (5,8). Studies of how sojourners acclimatize to altitude have been done for over a century by expeditions to the Alps, Andes, and Rockies. In 1911 Haldane, studying visitors to Pikes Peak (14,100 ft, 4267 m, 446 torr) suggested that one component of acclimatization might be the ability of the lungs to secrete oxygen from the alveoli into the blood (4), a concept which Barcroft disproved during his expedition to Cerro de Pasco (Peru) in 1921-2 (2).

Ten years later the International High Altitude Expedition to Chile (15) examined biochemical changes in the blood, pulmonary diffusion and shifts in the oxy-hemoglobin dissociation curve, in lifelong residents and in newcomers. No evidence of oxygen secretion was found and acclimatization was attributed to integrated changes in many body systems.

Members of the Silver Hut expedition of 1961 (20) lived at 5800 m (19,000 ft, 364 torr) for four months, and provided the first complete profile of changes in sea level natives living at high altitude; they made extensive studies of work capacity at altitude, including measurements of VO<sub>2</sub>Max up to 7620 m (25,000 ft, 282 torr). Their experience suggested that 5800 m was too high for permanent residence and predicted that at 8848 m work capacity would be so small that little work could be done, even by well acclimatized men. The Italian Everest Expedition in 1973 (3) confirmed these observations.

From 1967 to 1978 the Arctic Institute sponsored work at 5460 m (17,500 ft, 392 torr) on Mt. Logan in the Canadian Yukon; from this came the first reports of high altitude retinopathy, ataxia due to high altitude, and many reports of acute and long range exposure to the mountain environment (10).

In 1981 the American Medical Research Expedition to Everest (29) measured work capacity up to 6500 m (21,500 ft, 327 torr) and by projection confirmed the findings of the Silver Hut expedition (20). Venous samples at 8000 m (28,000 ft, 268 torr) and alveolar air samples on one subject at 8840 m were extrapolated to estimate blood gases on the summit of Everest.

All of these expeditions have produced a wealth of data on which rests much of our knowledge of acclimatization. Important observations have also come from lower laboratories on Pikes Peak, White Mountain, and Mt McKinley in North America and many stations in the Alps, Andes and Caucasus (8,9).

High mountains are the real world where man is exposed to many stresses which confound the response to hypoxia: cold, inadequate food, dehydration, sleeplessness, exhaustion, and anxiety. Recent tragedies in the Himalayas have underscored the synergism of these stresses with that of hypoxia. In order to assign proper weight to the favorable or adverse changes stimulated by hypoxia per se, it is necessary to isolate oxygen lack from other stresses. Such studies can be done in a low oxygen room (2) or in a decompression chamber, the latter being more practical for long term study. In addition certain crucial studies (eg. pulmonary diffusion, cardiac hemodynamics, and muscle biopsy) which are impossible, impractical or too

dangerous to the subject at extreme altitude, can be done in the decompression chamber. Since there is current speculation about the role of hypobaria per se at high altitude, as compared to normobaric hypoxia, the chamber is better able to simulate the hypobaric hypoxia found at high elevations.

In 1946 the Navy sponsored such a study, called Operation Everest during which four men lived in a decompression chamber for 34 days and two reached a barometric pressure of 235 torr breathing only air (11). Although these four men were not fully acclimatized, Operation Everest demonstrated the integration of changes which produces acclimatization. This study also demonstrated for the first time that men could work for short periods at 235 torr barometric pressure and thus might summit Mt. Everest (13).

#### OVERALL APPROACH

Many unanswered questions, new concepts and advanced technology stimulated interest in repeating this on a grander scale and in 1979 Operation Everest II was conceived as a study of acclimatization to 'pure' hypoxia. The design called for examination of changes in all parts of the oxygen transport system which result in acclimatization and thus permit work at altitudes which rapidly disable the sea level resident.

In addition to collecting a broad base of observations the following hypotheses were tested:

1. The hypoxic ventilatory response (HVR) is unchanged during acclimatization to high altitude.
2. Pulmonary gas exchange is increasingly impaired as altitude increases.
3. Pulmonary artery pressure increases as altitude increases and may be one factor limiting cardiac output.
4. The worsening of hypoxemia during exercise at altitude is due more to pulmonary diffusion limitations than to changes in the ventilation-perfusion ratio.
5. The increased oxygen uptake during exercise at altitude will depend more on polycythemia and tissue extraction and less on cardiac output than at sea level.
6. Exercise performance decreases progressively with increasing altitude, but the administration of oxygen does not restore performance to sea level values.
7. Left ventricular function as assessed by echocardiography becomes impaired during exercise at increasing altitude.
8. Oxygen delivery to muscle in acclimatized subjects at altitude is limited by a relative decrease in muscle blood flow secondary to blood viscosity.

9. The ventilatory and circulatory characteristics of persons able to reach 8848 m (29,028 ft, 253 torr) are distinctive.

10. Muscle strength will decrease more in weight bearing than in non-weight bearing muscles with increasing hypobaric hypoxia.

11. The following muscle ultrastructural changes will occur with increasing hypobaric hypoxia: increased capillary density, increased myoglobin, increased number of Type 1 fibers, changes in myosin composition and peptide pattern of sarcoplasmic reticulum, and increases in mitochondrial size and density.

12. The following transformations in muscle enzyme activity patterns will occur during progressive hypobaric hypoxia: a) increase in activity of citric acid cycle enzymes, b) increase in activity of beta oxidative enzymes, c) increase in activity of glycolytic enzymes, and d) increase in the oxidative potential.

13. Lactate concentration is reduced following maximal exercise in acclimatized subjects at altitude because of decreased muscle glycogen concentration, impaired glycolytic flux, and - in the presence of reduced bicarbonate, an impairment of lactate efflux from muscle.

14. During sleep at increasing altitude there will be progressive increase in periodic breathing and in number of apneas, an increase in hypoxemia and in the frequency of arrhythmias seen on the electrocardiograph.

15. The ventilatory response to CO<sub>2</sub> increases and the ventilatory response to hypoxia decreases during sleep at increasing altitudes.

#### METHODS

Crucial to the project were an adequate facility, dedicated and highly motivated subjects, and an expert scientific team, not to mention adequate funding. Planning and preparation took five years.

The Army Research Institute of Environmental Medicine (ARIEM) made available a suitable decompression chamber (Figure 1) which was L-shaped, consisting of one room 20 by 9 feet, connected to a smaller chamber measuring 9 by 12 feet. An intervening 9 by 7 foot lock or 'elevator' could be taken up or down independently to access both rooms. A 'pass-through' lock in each chamber made it possible to pass small items in or out. The larger room contained four double decker bunks, a treadmill, cycle ergometer, small table, water fountain and several chairs. In the lock was a toilet and shower and a climbing simulator called the Versaclimber.

Into the smaller chamber were crowded an 8 channel recorder, computer console, cycle ergometer and racks holding dry gas meter, spirometer, ear oximeter, electrocardiogram, and other instruments. Two mass spectrometers outside the chamber were fed from within, and other penetrations enabled transmission of dozens of individually isolated electrical signals. Both

chambers had oxygen outlets and emergency supplies as well as telephones and battery-operated communication systems. Three windows in each chamber permitted constant observation from outside. Humidity and temperature were kept at comfort levels (subjects preferred 84% and 72° F) and together with ventilation and altitude were readily controlled from a large master console which printed a record of these variables as well as of percentages of oxygen and carbon dioxide in the chamber each hour.

Barometric pressure in each chamber was recorded continuously by anaeroid barometers. Barometric pressure on the summit of Everest (8848 m as measured in 1988) customarily has been described as 240 torr, based on extrapolation of the ICAO pressure-altitude relationships (14). However, in 1981, the American Medical Research Expedition to Everest, using an accurate electronic barometer, determined the actual pressure to be 253 torr (29), a value predicted by Pugh (21) twenty years before. The deviation from the ICAO curve is present to a diminishing degree down to 6096 m where it becomes insignificant. We elected to follow the ICAO pressure/altitude curve except at the 'summit' because those values appear throughout the literature, and because they had not been measured at all intermediate altitudes by AMREE.

Since observers in this study wore oxygen continually in the chamber, and since ventilation at the very low pressure of extreme altitude was not adequate to remove all exhaled oxygen, the percentage of oxygen (which was continuously monitored in the chamber) at times rose as high as 22%. Therefore, in order to replicate the oxygen environment actually found on the summit of Everest, the "summit" studies were made at 240 torr with ambient air containing 22% oxygen, giving an ambient oxygen pressure of 53 torr. A similar correction was not needed at 7315 m because oxygen accumulated to an insignificant degree and the ICAO barometric pressure differed only slightly from that actually measured on the mountain (29). The values used in this study appear below:

Table One  
Barometric Pressure and Inspired Oxygen Percent and Tension according  
to the International Tables and as determined by the American Medical  
Research Expedition to Mt. Everest in 1981

Altitude m	Altitude ft	ICAO torr	FI02 %	PO2 torr	AMREE torr
0	0	760	20.9	159	760
1524	5000	632	20.9	132	632
3048	10000	523	20.9	109	523
4572	15000	429	20.9	90	429
5486	18000	380	20.9	79	380
6096	20000	349	20.9	73	352 *
6706	22000	321	20.9	67	335 *
7010	23000	307	20.9	64	320 *
7315	24000	294	20.9	61	310 *
7620	25000	282	20.9	59	300 *
8839	29000	240	22.0 #	53	253 *

- \* PB measured by AMREE taken from graph in (29)
- # Slight increase in % oxygen due to observers breathing oxygen and incomplete chamber ventilation.

ARIEM made available the complete operating crew necessary to operate the chamber 24 hours a day for more than 40 days, as well as a well equipped laboratory and professional staff, meeting rooms, photo-copying facilities, and complete support for the intense and concentrated effort. Twenty-six scientists involved in cardio-pulmonary or high altitude research at half a dozen universities joined the project.

Central to success were the subjects; on their willingness to be confined in a steel box for six weeks while cooperating in innumerable tests, many of which were painful and tiring, depended the success of the project. Sixty persons applied, 30 were thought suitable after initial screening, and 12 were invited. Selection was based on physical and mental fitness, athletic experience, a short questionnaire, eight letters of reference, and a long interview. This selection process had been successful during 12 years of the High Altitude Physiology Study on Mt Logan (10) in which over 100 subjects had participated. At the time of interview each was told the risks and rewards and the objectives and methods, and given the consent form to read and to show to his family and physician. Each received travel expenses, room and board and \$2500 for completion of the project.

All studies were approved by the ethics committees at McMaster University, University of Colorado, and University of California, San Diego, as well as by the Army Human Use Review Committee. Immediately before the study began the subjects gave informed consent after full explanation of the purpose, methods, and possible risks of all the studies

Eight male subjects and four alternates had been invited but several dropped out during the long wait, and the project began on September 27, 1985 with eight subjects and one alternate. Women were not included because hormonal cycles would fragment the already small group. The nine subjects can be briefly described as follows:

1. 27 year old resident in Family Practice; triathlon competitor but with little mountain experience. Height 196.8 cm. Weight 100.9 kg. BSA 2.35 m<sup>2</sup>.
2. 23 year old recent BA in micro-biology; little mountain experience. Withdrawn during baseline studies because of a fresh respiratory infection.
3. 28 year old house parent in home for handicapped; competitive distance runner; strong rock climber; unusual travel experience. Height 182.8 cm. Weight 75.2 kg. BSA 1.97 m<sup>2</sup>.
4. 27 year old pre-medical student; extensive mountain experience to 23000 feet; long distance (100 mile) runner; subject in many exercise research studies. Height 191.1 cm.

Weight 85.2 kg. BSA 2.14 m<sup>2</sup>.

5. 21 year old pre-medical student; competitive runner, expert in karate and martial arts; little climbing experience. Height 174.0 cm. Weight 58.5 kg. BSA 1.7 m<sup>2</sup>. Withdrawn at 25000 ft (282 torr) because of an hypoxic episode.

6. 31 year old medical student; competitive runner, skier; paramedic in mountain rescue; extensive rock climbing experience. Height 182.1 cm. Weight 84.6 kg. BSA 2.06 m<sup>2</sup>.

7. 27 year old bicycle mechanic; competitive cyclist and runner; no mountain experience. Height 178.7 cm. Weight 73. kg. BSA 1.91 m<sup>2</sup>. Withdrawn at 18000 ft (380 torr) because of an hypoxic episode.

8. 29 year old resident in Emergency Medicine; strong triathlon and marathon competitor; extensive mountain experience several times above 20000 feet. Height 171.4 cm. Weight 76.6 kg. BSA 1.89 m<sup>2</sup>.

9. 26 year old architect-designer; extensive back-packing and trekking but no high mountain experience; competitive swimmer and runner. Height 175.5 cm. Weight 73.5 kg. BSA 1.89 m<sup>2</sup>.

In selecting an appropriate rate of ascent it was necessary to balance the enervating effect of close confinement against the time needed to perfect acclimatization. No firm guidelines are recognized for an optimal ascent rate because of the large variation between individuals. An ascent profile like that of several successful Everest climbs, and similar to that of the 1946 study (11) was planned (Figure 2). After six days of baseline tests (three days inside the chamber) at sea level, the chamber was "climbed" to a higher simulated altitude between 0500 and 0600 each day. Several 'holds' of two to three days were inserted to enhance acclimatization and to accommodate more tests at the same altitude. Above 7010 m (23,000 ft 308 torr) subjects had difficulty sleeping and the ascent profile was modified by lowering chamber altitude each night 300-500 m below the daytime altitude.

On the 35th day after leaving sea level, all six were taken from 7620 m (25,000 ft, 282 torr) to 8840 m (2,9000 ft 240 torr) over a two hour period and remained there uneventfully for a half hour, while carefully monitored. During the final eight days subjects spent twelve hours each day at 7620 m (25,000 ft 282 torr), slept at 6700 m (23,000 ft 307 torr), and each day one of them was taken to 8848 m (29,198ft 22.0% oxygen, 240 torr) for several hours of tests, including Swan-Ganz catheterization studies done at 282 torr and, with the catheter in place, repeated at the summit.

To take maximum advantage of this unique opportunity, many other studies were added to the original program of examining the oxygen transport system; these are shown in Table 2. The experimental methods used in each protocol

are reported elsewhere.

Table 2  
Studies Performed during Operation Everest II showing  
altitude in meters

Alveolar Gas measurements	Daily
Swan-Ganz Cardiac Catheterization	SL 6096 7620 8839
Inert Gas Diffusing Capacity and V/Q	SL 4572 6096 7620 8839
Echocardiography, 12 lead EKG	Regularly
Hypoxic Ventilatory Response	SL 4572 7010 SL
Maximal Work Capacity	SL 3862 6096 7315 8839
Progressive Work (exhaustion): Muscle Biopsy	SL 5486 7620 SL
Muscle Neuro-Physiology	SL 6401 7620 SL
Clinical Examination	Daily
Psychometric Evaluation	Regularly
Fluid Intake/Output	Twice Daily
Dietary Intake	Daily
Sleep Studies	SL 4572 6096 7010 7620 SL
Ataxia	SL 4572 5486 7620 SL
Cerebral Blood Flow (Doppler)	SL 4572 5486 7620 SL
Retinal Photography	Regularly
Underwater Weighing	Before and After Ascent
CT Scan (leg and arm)	Before and After Ascent
Immune Status	SL 3048 7620
Venous Bloods (electrolytes etc)	Every 8 days
Blood Coagulation	SL 5486 7620

Changes in every portion of the oxygen transport system during gradual exposure to increasing altitude are the basis of the acclimatization process which we wished to examine. The centerpiece study was measurement of cardio-pulmonary dynamics by three cardiac catheterizations to provide accurate measurements of cardiac output, pulmonary artery and wedge pressures, and direct measurements on mixed venous blood (7). Simultaneously with the catheter studies the multiple inert gas technique (27) was used to measure pulmonary gas diffusion and thus determine the relationship between perfusion and ventilation. Mixed venous blood as well as arterial and peripheral venous blood were obtained. These studies were done at rest and during and immediately after graduated exercise on the cycle ergometer. Though the catheter studies placed heavy demands on both scientists and subjects, 19 of the 24 Swan-Ganz studies planned were completed satisfactorily. There were no mishaps.

Details of the cardiac catheterization and multiple inert gas studies are given elsewhere (7,17,28) and are only briefly summarized as follows. With the subject fasting and supine a Swan-Ganz catheter was floated through the subject's brachial artery into the heart and pulmonary artery, and arterial and venous lines were placed in the opposite arm. The subject then sat on the cycle ergometer, inhaled ambient air through a mouthpiece and exhaled through appropriate valves into a warmed mixing box and gasometer while an infusion containing six inert gases was running (28). This protocol was followed at SL, 6096 m (349 torr) and 7315 m (282 torr).

At 7315 m (25,000 feet, 282 torr), after resting and exercising hemodynamic measurements and inert gas diffusion measurements were completed, that subject was taken to 8840 M (29,028 ft, 240 torr) over a period of 30 to 60 minutes. There the Swan-Ganz, arterial and venous blood samples, and inert gas diffusion measurements were repeated. Usually the subject remained at the highest altitude for about two hours. The same procedure had already been done on all subjects at sea level and at 6706 m. Several subjects also went to "the summit" for echocardiography which took three hours or more.

In addition to the Swan-Ganz studies maximal exercise capacity (VO<sub>2</sub>Max) was measured at several altitudes on the Monark cycle ergometer with progressive increments in work load until oxygen uptake reached a plateau (Sutton in press).

In a different type of work, on a day several days distant from the maximal exercise study, muscle biochemistry and structure after progressive exercise to exhaustion were examined by muscle biopsies taken from the vastus lateralis before and after exercise on the ergometer increasing by steps to exhaustion. These samples were used to examine muscle structure, enzyme changes, myoglobin and mitochondrial content (Sutton, in preparation, Green, in preparation, MacDougall, in preparation).

Because arterial oxygenation is known to fall during sleep at altitude due to decreased and periodic breathing, sleep studies were done at several altitudes. Electro-encephalographic and canthal leads were placed to determine sleep stage, an ear oximeter was used to estimate arterial oxygen saturation, and a mouthpiece with valves to permit in-putting ambient air, a lower oxygen, or a high carbon dioxide gas mixture, and a mesh vest (Respitrace) with electrocardiographic leads and strain gage sensors was used to measure ventilatory expansion, rhythm, and the EKG. Two subjects were studied at a time, with the observer (wearing oxygen) in the chamber, controlling the recording (Anholm in preparation, Powles in preparation).

Protocols of other studies are included in specific reports by the responsible investigators, now nearing publication.

Dietary intake was carefully measured daily, and together with CAT scan, skin fold measurements, and underwater weighing before and after the study provided an estimate of caloric intake and distribution, and distribution of weight loss between lean and fat body mass. (Rose in press).

The condition of each subject was assessed each morning by brief interview and physical examination. Pulse and blood pressure were recorded while still in bed and again after standing for two minutes. Alveolar air samples were taken after an arterial needle had been placed, and immediately after the alveolar sample was obtained, arterial blood was drawn for gas analyses. Gas samples were analyzed by passing exhaled air through a mass spectrometer, and checked periodically by direct analysis of a bagged sample, (Malconian in preparation).

Each morning after emptying the bladder subjects were weighed. Twelve hour measurement of fluid intake and output as well as a complete dietary assessment and rough estimate of energy output were made each day.

Subjects were watched continuously by a crew of trained observers seated at windows outside the chamber, and were visited or talked with at length each afternoon by one of the doctors to obtain a clinical impression of their condition. Each subject completed an Environmental Symptoms Questionnaire twice daily (24).

#### GENERAL OBSERVATIONS

Above 4486 m (18,000 ft, 379 torr) subjects complained of headache, insomnia, anorexia, and above 6096 m, dyspnea. These symptoms improved during the three day 'hold' and were somewhat better above 7010 m. Pain and dryness in the throat and irritative cough bothered several. These are common complaints on high mountains. Only acetaminophen was permitted for headache. Three subjects were allowed occasional small doses of Halcion® (triazolam) for sleep above 5486 m. All were lethargic above 7315 m (24,000 ft, 293 torr) and it required real determination to continue daily exercises. All subjects felt and looked better, even at the summit, after exercising.

Though all subjects became more lethargic and exercised less as altitude increased, they were able to do progressive exercise to exhaustion and maximal oxygen uptake tests at 6706 m and 7620 m, although at only a third or less of the sea level load. (Cymerman, in preparation; Sutton, in press).

All subjects lost weight, mean = 7.4 kg, or 8.9% of body weight at sea level. Average weight loss was two kg (range 0.5 - 6) in the first two weeks and three kg (range 0.5 - 6) in the last three weeks. Caloric intake ranged from 2600 to 3600 Kcal (average 3100) the first week, falling to 1220 to 2300 (average 1900) in the final week despite free choice of meals. Fluid intake and output were consistently high for all subjects; sodium intake was slightly restricted (average 3.gm) in the first ten days to avoid fluid retention, but averaged 6 gm with free choice of food thereafter. One third of the weight lost was fat and two-thirds was lean tissue, as determined by CAT scan, hydrostatic weighing and 7 skinfold and 10 soft tissue circumferential measurements before and after ascent. (Rose, in press).

Sleep at altitude was disturbed for all subjects and REM sleep was significantly reduced. All subjects showed marked periodic breathing with apneas at altitude, unrelated to sleep stage. Severe arterial oxygen desaturation (50% or lower) was observed during sleep at extreme altitudes, and periodic breathing with prolonged apneas and some desaturation persisted after return to sea level. (Anholm and Powles, in preparation).

Three subjects experienced severe sore throats above 6100 m (20,000 ft) torr), despite the warmth (72-74 degrees Fahrenheit) and high humidity (70 to 84%). For two subjects this was severe enough to lead them (and us) to consider premature termination. On examination the throat was slightly reddened, without exudate, satellite nodes, or other gross pathology. Cultures were negative for pathogens. No form of treatment (lozenges, hard candy, humidifier in croup tent, various syrups) gave relief.

Scattered rales were occasionally heard in several individuals, and one subject was suspected of early pulmonary edema at 7010 m ((23,000 ft, 307

torr) but spontaneously diuresed and finished the study successfully. Three experienced observers, reading X-rays taken two hours after the project was completed determined that a different subject had mild pulmonary edema (though his lungs were clear to auscultation). However, three other readers felt that all X-rays were within normal limits.

Two subjects were removed prematurely. The first had a sudden episode of weakness, brief loss of consciousness and disorientation during the evening at 5486 m (18,000 ft, 379 torr); physical examination then and later showed no residual abnormalities. The second had a similar episode with brief aphasia during the morning at 7620 m (25,000 ft, 282 torr); his disorientation persisted for a minute or two after oxygen was given but examination then and on descent to sea level a few minutes later showed no residual neurological deficits. Both episodes resembled those often seen in persons abruptly exposed to such altitude. These two subjects had the two highest oxygen uptakes per kilogram body weight; they also showed the most erratic hypoxic ventilatory responses. These relationships and others will be analyzed by a powerful statistical program using the data base compiled from all data acquired.

Retinal hemorrhages were not seen below 7010 m (23,000 ft, 307 torr) but above this all subjects showed dilated, tortuous retinal vessels and retinal hemorrhages. Complete resolution of extensive hemorrhages in the subject brought down from 7620 m was documented within ten days after descent. (Rock, in preparation).

Systemic blood pressure, measured while still in bed each morning, increased slightly with altitude and when measured later in the day at rest before, during and after exercise studies, increased significantly with increasing altitude. (23). Orthostatic hypotension was occasionally noted at and above 7620 m. when the waking blood pressures were measured. Basal pulse rate varied widely between individuals.

The airlock made 250 trips and the 26 scientists spent a total of 1350 hours (range 1 - 188 hours) at altitude; 14 noted bends on one or more occasions above 5182 m (17,000 ft, 395 torr) although all pre-breathed oxygen for one hour. Only one, (a case of 'skin bends') was severe enough to terminate the stay at altitude. Incidence paralleled frequency of ascents as well as length of stay at altitude, and was roughly proportional to the work done. Two episodes of scintillating scotomata were noted (18). One scientist abruptly lost consciousness on two occasions at 8840 m when his oxygen supply was accidentally interrupted, dramatically demonstrating the difference between men adapted to altitude and those coming directly from sea level.

#### SPECIFIC OBSERVATIONS

"On the summit" maximal oxygen uptake (Cymerman, in preparation) averaged 1.2 l/min, slightly higher than that predicted by Pugh (20) and by West (30). Cardiac output and heart rate at high altitude were approximately those expected for the levels of exercise measured and did not appear to be a limiting factor (25). Cardiac function as measured by echocardiography and cardiogram monitoring was normal; echocardiography suggested some right

ventricular enlargement (25, Hultgren, in preparation).

The importance of increased ventilation in maintaining oxygenation was confirmed. The hypoxic ventilatory response was not blunted by the long period of hypoxia, and roughly paralleled the degree of acclimatization. (Schoene, in preparation). Pulmonary vascular resistance was increased and at the highest altitudes was not lowered by supplementary oxygen (7). By contrast, systemic vascular resistance was not significantly altered by increasing altitude.

A considerable but varying degree of ventilation/perfusion mismatch was found, and appeared to be an important factor limiting work at altitude. All subjects showed evidence of interstitial edema at the higher altitudes. In short, although the heart responded adequately to the challenge of severe hypoxia, the lungs did not (28).

"On the summit" (Table 3) arterial oxygen and carbon dioxide pressures were somewhat higher and arterial pH considerably lower than calculated by West (30). One subject showed an arterial CO<sub>2</sub> of 8.2 torr. During maximal exercise at the highest altitudes mixed venous oxygen fell to 10-12 vols%, half the minimum which could be achieved at sea level.

Table 3  
Alveolar and Arterial Gas levels

	AMREE n=1	OEII n=6	Rest	Rest	Exercise
Pb (torr)	253	240			
Ambient Oxygen (%)	20.94	22.0			
PIO <sub>2</sub> (torr)	53	53	53		
Alveolar O <sub>2</sub> (torr)	35	30			
Arterial O <sub>2</sub> (torr)	(28)	30	27		
Alveolar CO <sub>2</sub> (torr)	7.5	12			
Arterial CO <sub>2</sub> (torr)	(7.5)	11	11		
Arterial pH	(7.76)	7.57	7.52		

Data in parentheses were obtained by extrapolation from venous samples drawn later at lower altitude.

Alveolar and arterial gas samples obtained on awakening showed that alveolar CO<sub>2</sub> was essentially the same as arterial CO<sub>2</sub> at all altitudes; alveolar O<sub>2</sub> was several torr higher than arterial O<sub>2</sub> up to 4267 m (14,000 feet 446 torr). Above this altitude alveolar and arterial samples obtained simultaneously showed that arterial O<sub>2</sub> was either the same or slightly lower than the arterial O<sub>2</sub>. By contrast alveolar and arterial gas samples taken in the course of the day showed alveolar oxygen tensions slightly higher than arterial oxygen tensions, a gradient which became slightly smaller as altitude increased. No simultaneous samples of alveolar and arterial oxygen have previously been obtained above 14,000 feet, either from sojourners or from acclimatized residents. (Malconian, in preparation).

The number of subjects studied was small because of the complexity of such a study, but the data obtained are considered reliable. No objective measures of acclimatization are recognized, and although these subjects may not have been perfectly acclimatized after 40 days of gradually increasing altitude, in our judgment they were capable of climbing to the summit of Everest. Possibly the long confinement and inability to exercise as much as they were accustomed to may have contributed to anorexia and weight loss and may have impeded acclimatization. It is also conceivable that the compounding effect of the stresses in the mountain environment may stimulate rather than hinder the process, but these are only speculations.

\* \* \* \* \*

The major findings of Operation Everest II may be summarized as follows:

#### HEMODYNAMIC DATA

##### As altitude increased:

Right atrial and wedge pressures remained normal.

Resting pulmonary artery pressure increased from 15 to 34 torr.

Cardiac output for a given oxygen uptake was maintained.

During work: pulmonary artery pressure increased from 33 to 54 torr.

At rest: pulmonary vascular resistance increased from 1.2 to 4.3 Wood units.

At altitude: 100% oxygen lowered CO and PAP but not PVR.

Systemic blood pressure increased slightly.

#### VENTILATION

Increasing ventilation is the most effective change ensuring adequate tissue oxygenation during acclimatization.

At the highest altitudes, ventilatory drive was not depressed.

As altitude increased there was variable but increasing V/Q mismatch which correlated with increasing pulmonary artery pressure.

This was consistent with increasing interstitial alveolar edema.

At extreme altitude the lung is a major factor in limiting maximum oxygen uptake.

#### WORK

The relationship of oxygen uptake to workload was consistent throughout.

Maximal oxygen uptake fell from 4.13 l/min at SL to 1.2 l/min at Pb 240.

Maximal oxygen uptake decreased by 75% from SL to 240 torr.

Anaerobic metabolism contributed less energy as altitude increased.

Acclimatization to extreme hypoxia did not maximize oxidative function.

Peak blood lactate during exercise at extreme altitude decreased perhaps due to reduction of glycolytic flux rate.

#### OXYGEN TRANSPORT AND DELIVERY

A given oxygen uptake was achieved by lowering mixed venous oxygen in preference to increasing cardiac output.

Number of capillaries per muscle cross sectional area increased.

Number of capillaries per muscle fibre did not change.

Myoglobin in both Type I and II muscle did not change. Oxygen transport at extreme altitude is defended principally by increased ventilation and decreased mixed venous oxygen. During exercise at altitude mixed venous PO<sub>2</sub> was between 10 and 14 torr; at SL it was above 20 torr. At SL more than 80% of oxygen O<sub>2</sub> delivered was used. At Pb 347 and 282 extraction was similar but was less at Pb 240. Tissue diffusion may be limiting at extreme altitude.

#### HEART

Despite RV systolic hypertension, severe hypoxemia, and reduced preload, LV function was sustained or even enhanced. Heart rate for a given oxygen uptake increased with altitude and was only slightly slowed by breathing oxygen. Systemic BP increased as altitude increased, and increased further with 100% oxygen suggesting different control mechanisms between pulmonary and systemic BP. Moderate right ventricular enlargement, paradoxical septal motion, and well preserved systolic emptying were apparent on echocardiogram at extreme altitude. The heart was not a limiting factor at extreme altitude.

#### NUTRITION

Although ample appetizing and nourishing food was provided, appetites and food intake declined. All subjects lost more weight than accounted for by balancing calculated energy expenditures against actual caloric intake. CT scans and hydrostatic weighing showed that two thirds of the weight loss was muscle mass.

\* \* \* \* \*

The work summarized here is being reported in a series of papers in several technical journals, under the overall title of "Operation Everest II". The large volume of data collected has been assembled in a computerized data bank for further study by others. Specific data and conclusions for each study are given in the individual papers listed in the appendix.

The opinions expressed in this report are those of the author and should not be construed as those of the Department of the Army. The project was sponsored by the Arctic Institute of North America and funded by the US Army Research and Development Command (Contract No. DAMD17-85-C-5206).

Principal Investigators were Charles S Houston, John R Sutton and Allen Cymerman. Participating scientists were: James Alexander, Maureen Andrew, James Anholm, Louis Banderet, Dick Burse, Jonathan Carter, Geoff Coates, Howard Donner, Ulrich Duncan, Charles Fulco, Scott Garner, Howard Green, Bertron Groves, Harriet Gustaffson, Peter Hackett, Duncan MacDougall, Mark Malconian, Richard Meehan, Hugh O'Brodovich, Peter Powles, John Reeves, Rob Roach, Paul Rock, Madeleine Rose, Robert Schoene, Jose Suarez, Brenda

Townes, Darlene Tyler, Peter Wagner, John West, Patricia Young. To the many others we express our gratitude, particularly to James Devine and members of the chamber operating crew. The subjects deserve special thanks for without them the project would have been impossible: Steve Andracki, Peter Bangs, Roger Gough, Andy Lapkass, Eric Meyer, Steve Painter, Ben Schiffrin, Greg Welton, and Chip Woodland.

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#### ABSTRACTS

Several dozen abstracts have appeared in various publications, and in programs for numerous symposia.

#### SYMPOSIA ON OPERATION EVEREST II

Findings from Operation Everest II have been the subject of several symposia held in conjunction with the following large international meetings:

American College of Sports Medicine, Indianapolis, May 28, 1986.

American Physiological Society, New Orleans, October 8 and 9 1986.

Canadian Association of Sports Sciences, Lake Louise, October 7, 1987.

Fifth International Hypoxia Symposium, Lake Louise, February 15, 1987.

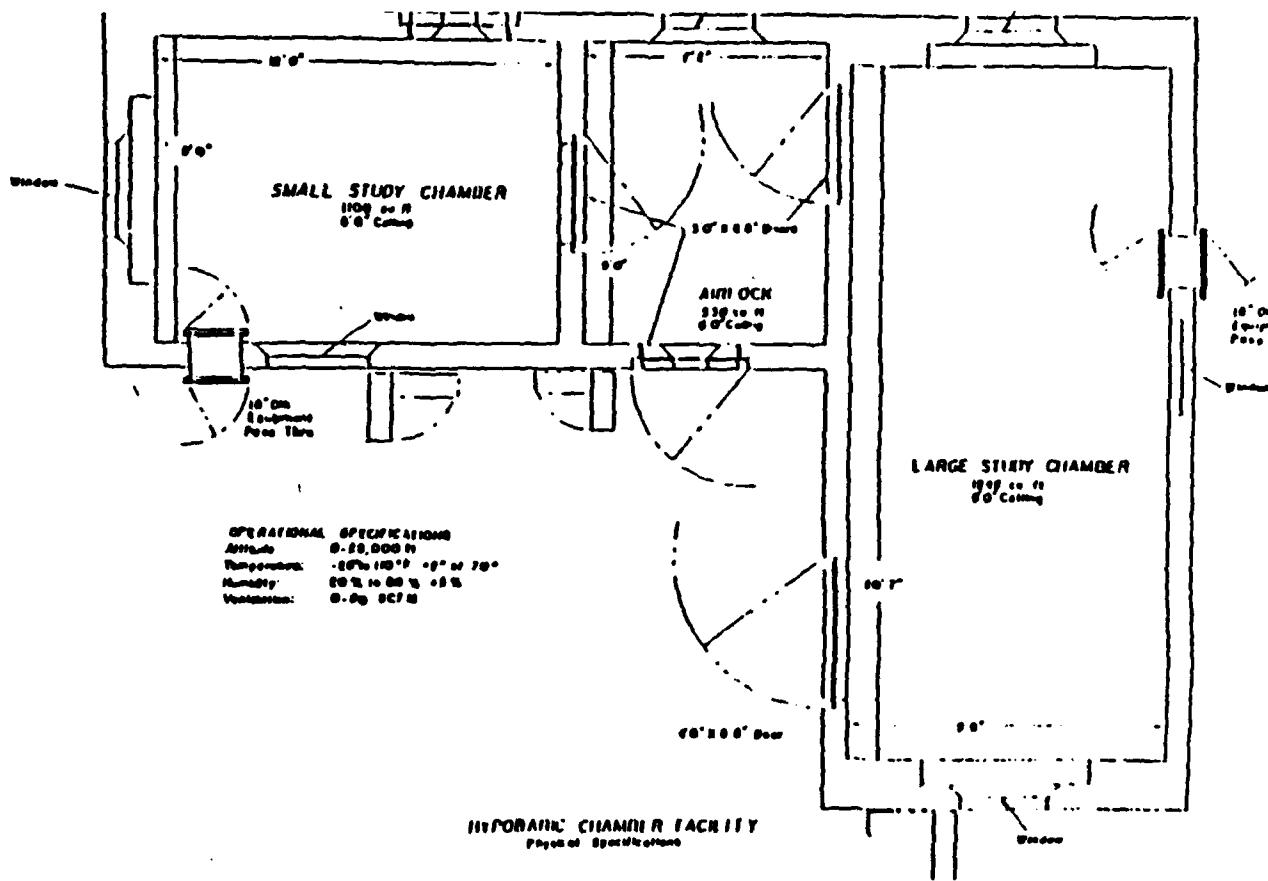


FIG. 1. Decompression chamber floor plan.

Barometric Pressure  
and Altitude

$P_B$       m      ft  
(mmHg)            $\times 10^3$

OPERATION EVEREST II  
ASCENT PROFILE

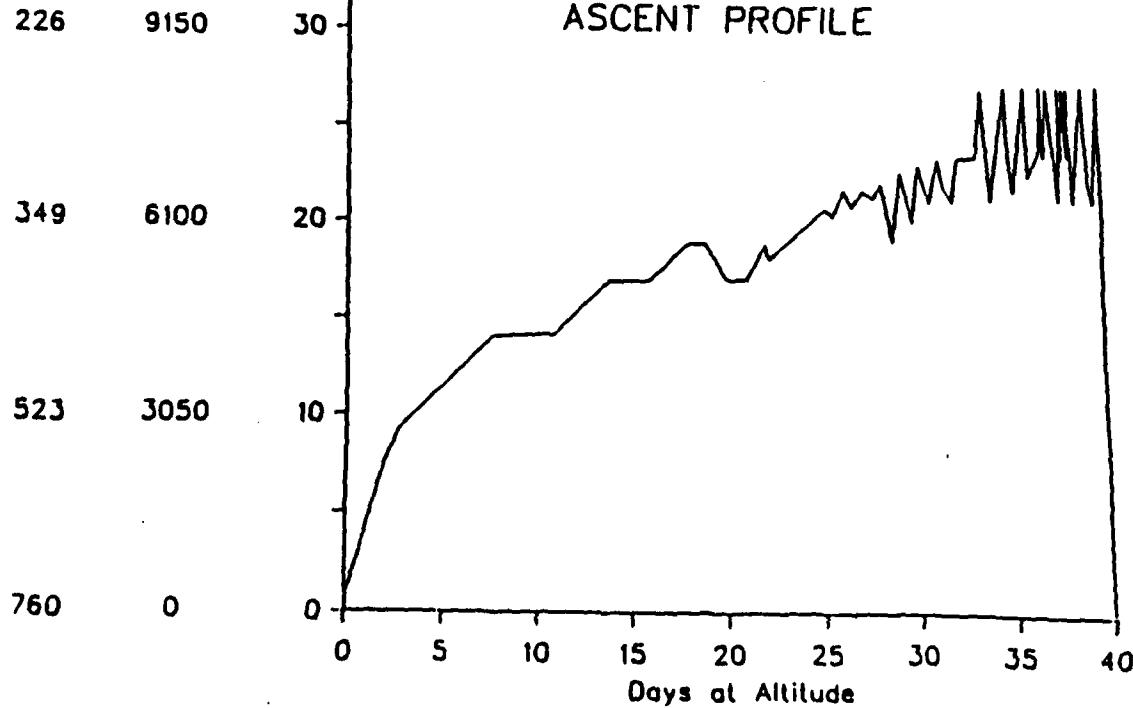


FIG. 2. Rate of metric pressure.